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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/334,969	06/17/1999	BENT KARSTEN JAKOBSEN	102286.410	5926
7590		06/22/2004	EXAMINER	
HOLLIE L BAKER		DIBRINO, MARIANNE NMN		
HALE AND DORR LLP		ART UNIT		
60 STATE STREET		PAPER NUMBER		
BOSTON, MA 02109		1644		

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action**Application No.**

09/334,969

Applicant(s)

JAKOBSEN ET AL.

Examiner

DiBrino Marianne

Art Unit

1644

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

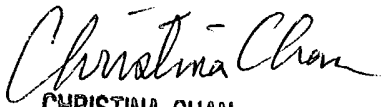
Claim(s) rejected: 1-11, 14-27 and 34-36.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☒ Other: See Continuation Sheet



Continuation of 10. Other: The rejections of record in the Office Action mailed 12/19/03 stand for the reasons of record in the said Office Action. Applicant's arguments in Applicant's Amendment filed 3/12/04 are of record and have been fully considered, but are not persuasive. With regard to Applicant's comments on Garboczi et al in the paragraph spanning pages 9 and 10 in Applicant's amendment filed 3/12/04, it is the Examiner's position that although the calculated molecular mass of the heterodimer is 50.2 kDa, shape affects the mobility of a molecule through a sieving gel, thus all the molecules in one gel must have similar shapes for valid comparison, and the elution of a complex from a sieving gel in the 40kDa fraction was able to bind MHC/peptide with specificity. It is the Examiner's further position that that the said Office Action did not suggest that Figure 4 relates to a native gel. It is the Examiner's position that Garboczi et al teach on page 5409 at the paragraph spanning columns 1 and 2, that if in the absence of the interchain disulfide bond, low affinities between some pairings of the alpha and beta chains should limit heterodimer stability, high concentrations of the polypeptides now available from bacterial expression could be used to overcome this. Garboczi et al teach on page 5404 at the first full paragraph the advantage of expressing alpha and beta chains without the cysteines that form the interchain disulfide bond when expressing and or refolding together the two said chains. Applicant states in the said amendment on page 9 "The SDS in this gel is, of course, expected to denature the TCR alpha and beta chains", referring to an SDS-PAGE gel. Golden et al teach improvement in yield of coexpressed alpha and beta chain of a murine TCR, different from the human TCR produced by Garboczi et al, by creation of leucine zipper fusion alpha and beta sequences. The yield taught by Golden et al in E. coli is 20X lower than the yield taught by Garboczi et al in E. coli. Regarding Applicant's comments about Golden et al teaching away from the present invention with regard to exclusion of the interchain disulfide bond forming cysteines, Applicant states in the said amendment of page 9 with regard to SDS-PAGE gel analysis, that "The SDS in this gel ...is expected to denature TCR alpha and beta chains [and gels that are not native gels such as the one referred to by Applicant in Golden et al] provides no assistance in answering the question of the non-covalent association of the TCR chains under native conditions, one way or another".


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